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# The Role of the Dialysate Flow Rate in Haemodialysis

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Additional information is available at the end of the chapter

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## 1. Introduction

Modern dialysis devices such as the Fresenius FMC 5008 allow the relationship between the flow rates of blood  $Q_B$  and dialysate  $Q_D$  to be fixed at a set ratio (e.g.  $Q_D=1.2 Q_B$  oder  $Q_D=1.5 Q_B$ ). The FMC-Genius®-Therapy System, which uses a double-sided peristaltic pump for both the patient's blood and the dialysis fluid (50...350 ml/min), even allows a ratio of  $Q_B=Q_D$ .

The relationship between the effectiveness of haemodialysis on the one hand, and the flows of blood and dialysate on the other, is guided by physical principles. These principles have been known for some time and have been widely discussed in the literature [1]. However, the fact that dialysis machines are completely automated makes it easy to neglect the underlying principles, so much so that knowledge of these may at times be lacking. There are also financial pressures that result in a desire to economise on water and dialysate concentrate, and a desire to work with as low a dialysate flow rate as possible.

The following sections will provide a brief summary of the theory behind the principles involved. In vitro and in vivo testing results from some of the more commonly available dialysers are used to provide a clearer picture of the theoretical principles involved. These measurements show that in spite of modern dialysis membranes and structural changes, it is not in fact possible to reduce the dialysate flow rate without also reducing the dialysis dose.

## 2. Theoretical principles

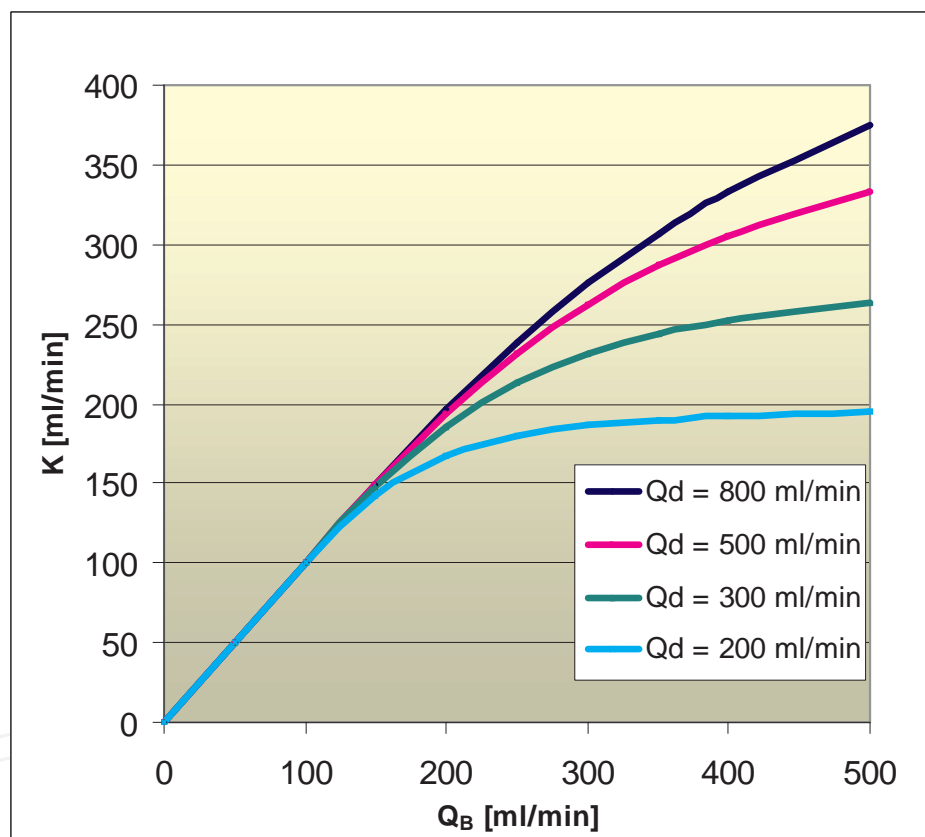
The connection between the dialyser's technical parameters and the flow rates involved ( $Q_B$ ,  $Q_D$  in the counter current flow) is based on the following relationship [1]:

$$\begin{aligned}
 K_O A &= \frac{Q_B}{(1 - Q_B / Q_D)} \ln \left[ \frac{1 - K / Q_D}{1 - K / Q_B} \right] & \text{a} \\
 K_O A &= \frac{K}{(1 - K / Q_B)} & \text{b}
 \end{aligned}
 \tag{1}$$

For  $Q_B = Q_D$  the following applies:  $K_O A = \frac{K}{1 - K / Q_B}$

where  $K_O$  is the "overall mass transfer coefficient" and  $A$  is the dialyser membrane surface area.

In dialysis log sheets, the  $K_O A$ -value is usually recorded for urea, thus allowing the calculation of urea-clearance in relation to blood and dialysate flow rates.



**Figure 1.** Dependence of clearance  $K$  on the flow rates of blood  $Q_B$  and dialysate  $Q_D$  ( $K_O A = 1000$  ml/min)

Fig. 1 shows how clearance rate  $K$ , derived from the  $K_O A$  value for a low molecular substance (urea), changes in relation to blood flow rates, with the relationship demonstrated at different dialysate flow rates, and for a high-flux dialyser. At low dialysate flow rates, the dialysate compartment soon becomes saturated, leading to a large reduction in the concentration gradient. This in turn means that an increase in blood flow will no longer produce a substantial improvement in the rate of clearance. It is only when the dialysate flow rate is high enough for the substance in question to be removed quickly from the dialysate chamber that a higher

blood flow rate can produce substantial improvements in the rate of clearance. This is effectively only ever the case when the dialysate flow rate  $Q_D$  is at least 1.5...2.0 times as high as the blood flow rate,  $Q_B$ .

This theoretical relationship requires the KoA value to be constant for all dialysate and blood flow rates. This does of course not apply in practice in cases where the total surface area of the dialyser's fibre bundle is not completely bathed in dialysate. This may happen when low dialysate flow rates lead to preferential channels being formed (please also refer to Sections 3 and 4). In the presence of relatively low dialysate flow rates, therefore, clearance values which may seem possible in theory are in fact unachievable in practice.

It must be emphasised, however, that these observations only apply to transport by diffusion, the most important transport mechanism for low molecular weight substances such as urea, creatinine and phosphate. As far as larger molecules are concerned, it is convective solute transport that becomes increasingly important as the molecular weight of the solute increases. With regard to the manner in which the overall clearance  $K_T$  depends on both of these mechanisms, only an incomplete explanation can be provided. Werynski's equation [2] offers a reasonable approach:

$$K_T = K_{diff} + TrQ_F \text{ where } Tr = S(1 - K_{diff} / Q_{Bi}) \quad (2)$$

Tr: transmittance coefficient; S: sieving coefficient;  $Q_F$ : ultrafiltration rate

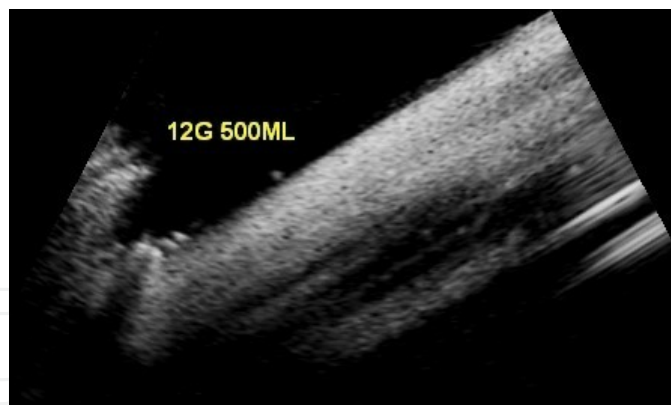
As the value for clearance by diffusion,  $K_{diff}$  in relation to blood flow rate,  $Q_B$ , decreases, the transmittance coefficient approaches the sieving coefficient, and the overall clearance  $K_T$  is effectively determined by the ultrafiltration rate  $Q_F$ . It follows that the dialysate flow rate  $Q_D$  has less significance with regard to larger molecules than it does with regard to smaller ones.

### 3. Structural changes to allow optimisation of the dialysate compartment

Fig. 2 shows an enhanced ultrasound image depicting an unfortunate case of channelling observed in a test dialyser during the inflow of dialysate.

In order to avoid, or at least reduce, this channelling phenomenon, different structural alterations are commonly applied:

- Flat sheet arrangement of hollow fibres
- Wave-shaped hollow fibres (Moiré structure)
- Spacer yarns
- Pinnacle structure in the dialysate inflow and outflow areas.



**Figure 2.** Enhanced ultrasound image of inflowing dialysate at  $Q_D=500$  ml/min (Dialyser Altair 12G, US-machine Logic 7, GE Medical Systems, contrast agent: Optison®)

Although a number of manufacturers at one point utilised flat-plate arrangements of interwoven hollow fibres in their dialysers (e.g. HFD 1.0 by MLW), this method has since been abandoned—probably due to cost reasons. Almost all manufacturers prefer the Moiré structure of fibres in order to obtain adequate spacing. In some instances—and sometimes in addition to the Moiré structure—spacing filaments (spacer yarns) are added (e.g. Asahi PAN650SF, MTP VitaPES). Although these measures ensure improved dialysate flow distribution within the cross-sectional area of the dialyser, in vitro testing using CT imaging has revealed that some preferential channelling through peripheral areas of the dialysate compartment remains [3, 4, 5]. With its FX series, Fresenius Medical Care followed a different path. Via a pinnacle structure in the inflow and outflow tracts, the dialysate is forced into even distribution across the entire surface area [6]. In the early days, dialyser technology included a number of devices whose inlet and outlet headers were fitted diagonally to improve the distribution of dialysate across the fibre bundle (e.g. EMC TriEx). For reasons unknown, this very simple solution did not prevail.

#### 4. In vitro analyses examining dialysate flow dependence of solute clearance

A dialysis machine (FMC 4008) was used to perform in vitro measurements of clearance rates in accordance with standard ISO 8637. A batch of 7.0 L stirred and thermostatically warmed dialysis liquid served as “blood” with dissolved urea and vitamin B12 as test substances. Measurements were carried out at different dialysate and blood flow rates, with each dialysate flow rate ( $Q_D=300, 500, 800$  ml/min) being measured at blood flow rate settings of  $Q_B=100, 200, 300, 400$  ml/min. These measurements were repeated for the 3 different types of dialysers.

Clearance data were obtained for one small molecule (urea, relative molecular weight=60) and one larger molecule (vitamin B12, relative molecular weight=1357).  $K_oA$  values were then calculated according to GI. 1a, b and compared with the values provided by the manufacturers.

Dialyser	Membrane	Manufacturer	KoA urea [ml/min]
FDY-150 GW	PEPA®	Nikkiso	874
FX 60	Helixone®	FMC	967
VitaPES 150HF	Purema®	MTP Pirna	1167

Table 1. List of dialysers used for in vitro testing

Fig. 3 shows that the measured characteristics generally followed the theoretical model (refer to Fig. 1). However, the clearance rates calculated using the catalogue KOA values were not achieved at low dialysate flow rates. It was not until  $Q_D=800$  ml/min that the values obtained managed to improve slightly on the ones provided. Similar curves were obtained for the other types of dialysers. The KoA values calculated from clearance,  $Q_B$  and  $Q_D$  were dependent upon both blood flow rate of blood and dialysate flow rate. In an ideal scenario, this kind of relationship should not exist. The overall mass transfer coefficient,  $K_o$ , is a physical characteristic of the fibre bundle and does not vary with the flow rates that might exist on the blood-side or the dialysate-side. Different KoA values in the presence of different flow rates can be easily explained provided if the effective surface area  $A$ , which is involved in solute transport, fails to remain constant. Values that may be theoretically possible will of course not be achieved in situations where a low dialysate flow rate results in sections of the fibre bundle not being immersed in dialysate. Fig. 4 shows that the KoA value calculated for the dialyser FDY150GW depends upon the dialysate flow rate.

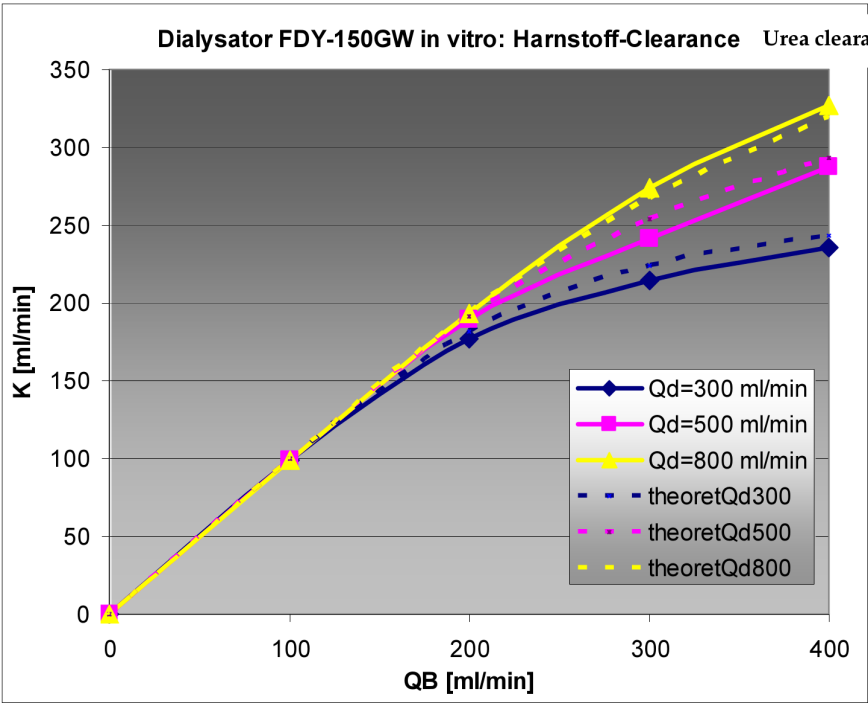
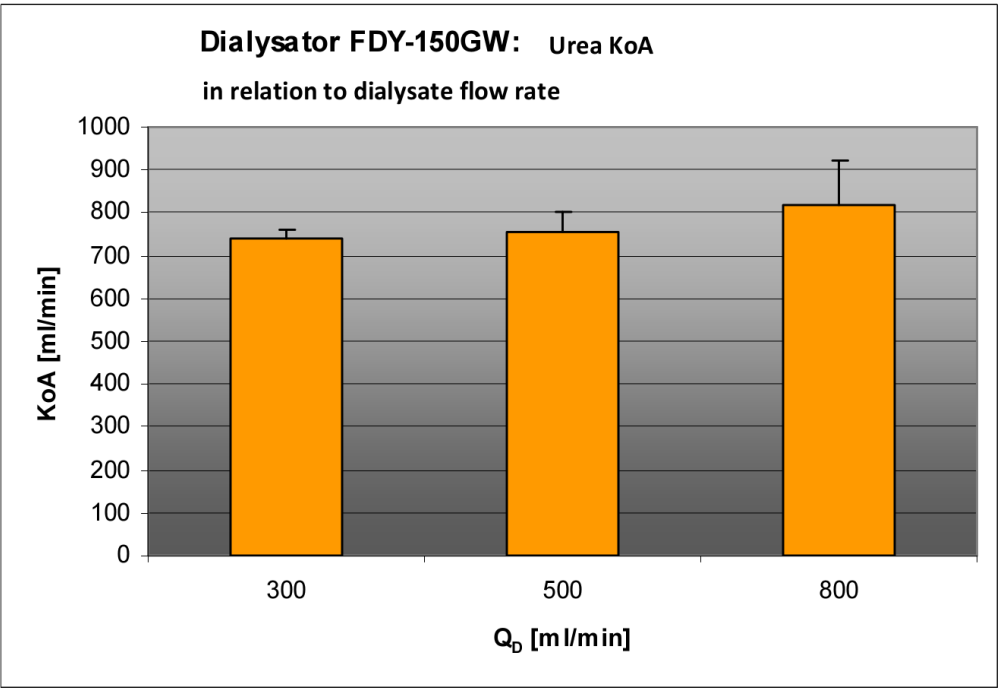


Figure 3. Comparison of measured urea clearance values and urea clearance values derived from KoA data provided by the manufacturers.



**Figure 4.** KoA values calculated based on clearance,  $Q_D$  and  $Q_B$ , using the dialyser FDY150GW as an example

$Q_D$ /dialyser type	FDY150GW	FX60	VitaPES150HF
$Q_D = 300$ ml/min	740 ± 21	728 ± 26	792 ± 64
$Q_D = 500$ ml/min	753 ± 49	751 ± 42	936 ± 34
$Q_D = 800$ ml/min	817 ± 104	756 ± 70	1063 ± 106
Catalogue value	874	937	1167

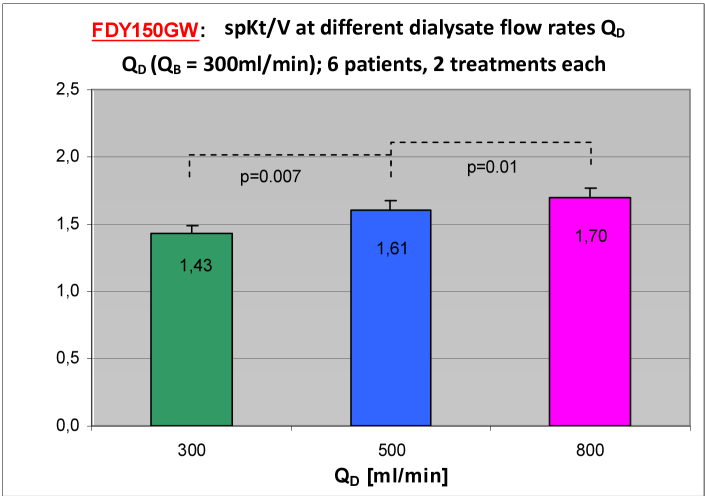
**Table 2.** In vitro KoA values [ml/min] for urea at different dialysate flow rates  $Q_D$  (mean values for different blood flow rates  $Q_B$ )

The dialyser FX60 showed the lowest degree of dialysate flow rate dependence of the KoA value. Although this was likely to be due to improved dialysate flow, the device still failed to achieve the manufacturer's catalogue value.

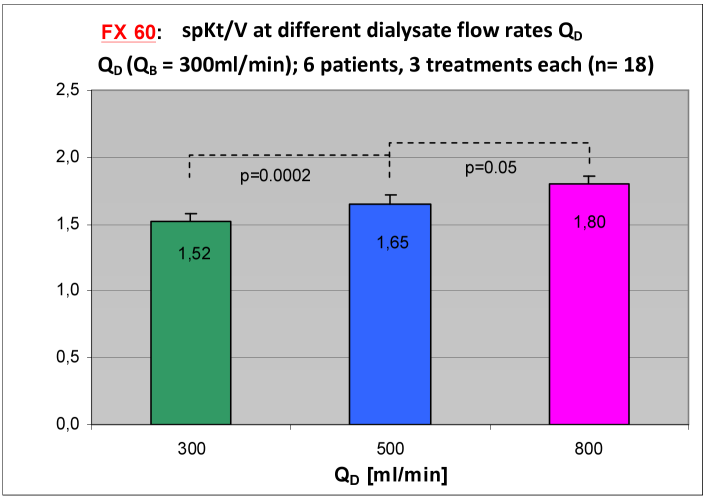
In summary, it has to be concluded that even modern high flux dialysers providing structural changes to optimise dialysate flow do not manage to negate the underlying relationship between the flow rates of blood and dialysate. Furthermore, full use of the fibre bundle's effective surface area  $A$  can only be guaranteed at high dialysate flow rates of around 800ml/min. Whilst this mirrors the results obtained by Leypolt [7], it contradicts the assumptions made by Golper and Ward, who concluded that structural improvements have made high dialysate flow rates unnecessary.

5. In vivo analyses examining the dialysate flow rate dependence of solute clearance

Naturally, in vitro investigations involving dialysers have to be treated with caution, with results not directly transferable to the clinical dialysis setting. Due to its viscosity and non-Newtonian flow properties, blood is a much more complex substance than an aqueous test solution. Also, unlike dialyser clearance rates, in vivo clearance rates depend upon physiological factors such as compartmentalisation of the blood and the uraemic toxins contained therein, fistula recirculation, cardiopulmonary recirculation, individual differences in haematocrit, as well as differences in protein and lipid concentrations. In spite of this, when looking at a sufficiently large number of patients and dialyses treatments, the basic principles discussed above should be mirrored in the clinical dialysis setting.

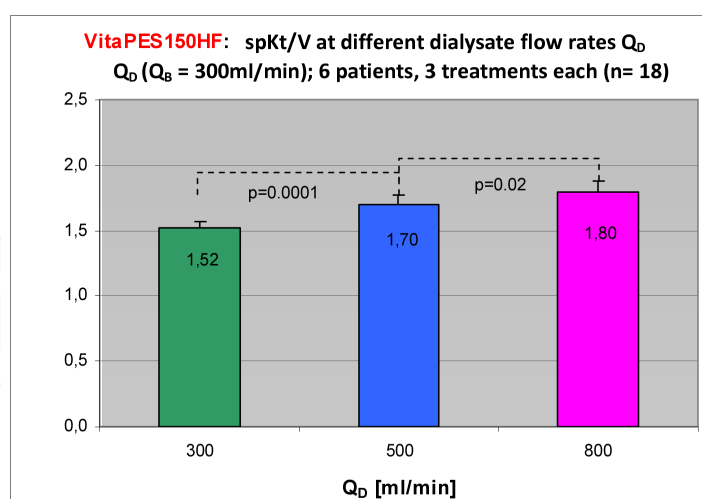


(a)



(b)





(c)

**Figure 5.** (a): Dialysate flow rate dependence of the spKt/V value in dialyser FDY150GW (b): Dialysate flow rate dependence of the spKt/V value in dialyser FX60 (c): Dialysate flow rate dependence of the spKt/V value in dialyser VitaPES150HF

At a constant blood flow rate ( $Q_B = 300$  ml/min), a group of 6 patients received three treatments each at  $Q_D = 300, 500$  and  $800$  ml/min, with each set repeated for each of the 3 types of dialysers tested in vitro. In order to assess the effectiveness of treatment, the urea reduction ratio, single pool Kt/V (spKt/V) and equilibrated Kt/V (eqKt/V) were obtained (Daugirdas formula). In addition, OCM data were obtained for the dialysis machine FMC 5008 (Eff.Kt, Eff.Kt/V).

The figures show (as do the urea reduction ratios and eqKt/V results) that each step increase in dialysate flow can significantly improve the effectiveness of haemodialysis.

The interesting question for dialysis patients is of course the exact impact this may have on treatment time. A sample calculation using results from the FX60 dialyser will demonstrate this (see Table 3).

Patient No.	$BW_{opt}$ kg	$V_{calc}$ L	$K_{300}$ ml/min	$K_{500}$ ml/min	$K_{800}$ ml/min	$KtV_{300}$	$t_{300}$ min	$t_{calc500}$ min	$t_{calc800}$ min	$t_{300}-t_{500}$ min	$t_{300}-t_{800}$ min
1	75.0	37.1	186	199	209	1.18	240	220	209	20	31
2	60.0	26.9	181	197	207	1.57	240	215	204	25	36
3	66.0	23.0	158	190	202	1.35	180	163	154	17	26
4	75.5	33.6	184	202	216	1.71	300	285	267	15	33
5	69.0	31.8	173	199	207	1.36	240	217	208	23	32
6	69.5	27.9	178	188	201	1.93	300	287	268	13	32

( $V_{calc}$  from OCM EffKt and measured Kt/V;  $t_{calc} = Kt/V(QD300) \cdot V/K$ )

**Table 3.** Time saved by using a dialysate flow rate of  $Q_D = 500$  ml/min or  $Q_D = 800$  ml/min instead of a dialysate flow rate of  $Q_D = 300$  ml/min

The same Kt/V value achieved at a dialysate flow rate  $Q_D=300$  ml/min can be achieved at a dialysate flow rate of  $Q_D=500$  ml/min, whilst treatment time can be reduced by between 13 and 25 minutes, depending on the individual patient's body mass and clearance. If a dialysate flow rate of  $Q_D=800$  ml/min is used, treatment time will be reduced accordingly, namely by 26-36 min. Treatment time reduction of this order is certainly of interest to patients and should be able to outweigh the slight increase in costs incurred by higher dialysate flow rates. Naturally, if treatment time remains unchanged, a higher dialysate flow rate can also be used to improve the Kt/V value-as depicted in Fig. 5.

## 6. Summary

In vitro measurements obtained from a number of different modern high flux dialysers show that the characteristics "Clearance ( $Q_B$ ,  $Q_D$ )" manage to closely match theoretical scenarios of expected interdependence. However, in spite of a number of different structural improvements, the KoA value remains dependent upon the dialysate flow rate. A higher dialysate flow rate of around 800 ml/min ensures that the fibre bundle is bathed more evenly in dialysate, thus improving the effectiveness of dialysis.

In vivo investigations confirm that increases in dialysate flow rates are likely to produce significantly improved Kt/V values.

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